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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,802	04/18/2005	Patrick Edward Crawley	PA/4-32729A	3683

1095 7590 10/12/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
CHU, YONG LIANG	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
10/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,802	CRAWLEY ET AL.	
	Examiner	Art Unit	
	Yong Chu	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, and 4-9 are pending in the instant application.

Information Disclosure Statement

Applicants' Information Disclosure Statement, filed 04/18/2005, has been considered. Please refer to Applicant's copy of the PTO-1449 submitted herewith.

Priority

This application is a 371 of PCT/EP03/11498 filed 10/16/2003, and claims the priority of U.K. Patent Applications 0224198.2 filed 10/17/2002.

Status of the Claims

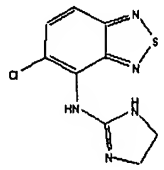
Claims 1 and 4-9 will be examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "derivative" in "5-alkyl-2-arylaminophenylacetic acid derivative" renders claim 6 indefinite, because it is not clear what derivative is.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claimed compound "5-chloro-4-(2-imidazol-2-ylamine)-2,1,3-benzothiadiazole" does not come with a chemical formula under ChemDraw software. The Examiner interprets the compound as  . Appropriate action is required.

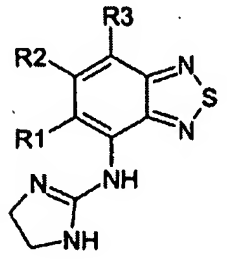
Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 5 are rejected under 35 U.S.C. 102 (b) as being anticipated by Sirdalud Ternelin Asia-Pacific Study Group, *Current Therapeutic Research*, **1998**, Vol. 59, 1, pp. 13-22, ("the *Sirdalud Study*").

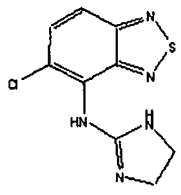
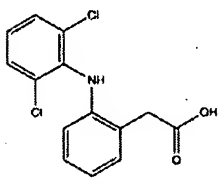
Applicants' claims relate to a pharmaceutical composition for treatment of pain, which comprises in combination a benzothiadiazole derivative of formula (I)



wherein each R1, R2 and R3 independently, is hydrogen, halogen, C_1-C_7 alkyl, C_1-C_7 alkoxy, nitro, cyano, hydroxy or C_1-C_7 alkylthio;
and a COX-2 inhibitor for simultaneous, sequential or separate use

and a method of treating a patient suffering from pain comprising administering to the patient an effective amount of the pharmaceutical composition thereof according to claim 1.

The *Sirdalud Study* discloses a pharmaceutical regimen of tizanidine plus diclofenac and a clinical study using tizanidine plus diclofenac to treat patient with low-back pain.

According to Wikipedia encyclopedia, "tizanidine" is the generic name of the compound of Formula  (CAS RN 51322-75-9), also called "Zanaflex" or " Sirdalud". "Diclofenac" is the generic name of the compound of Formula  (CAS RN 15307-86-5), a COX-2 inhibitor. See Wikipedia encyclopedia on-line version. The prior art anticipates claims 1, 4, and 5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

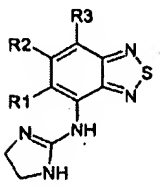
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4, 5, 7, and 9 are rejected under 35 U.S.C. 103 (a) as unpatentable over a publication by Sirdalud Ternelin Asia-Pacific Study Group, *Current Therapeutic Research*, **1998**, Vol. 59, 1, pp. 13-22, ("the *Sirdalud Study*").

Applicants' claims relate to a pharmaceutical composition for treatment of pain, which comprises in combination a benzothiadiazole derivative of formula (I)

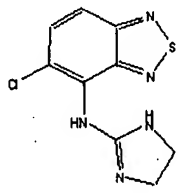
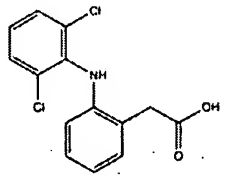


wherein each R1, R2 and R3 independently, is hydrogen, halogen, C_1-C_7 alkyl, C_1-C_7 alkoxy, nitro, cyano, hydroxy or C_1-C_7 alkylthio;
and a COX-2 inhibitor for simultaneous, sequential or separate use

and a method of treating a patient suffering from pain comprising administering to the patient an effective amount of the pharmaceutical composition thereof according to claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)

The *Sirdalud Study* discloses a pharmaceutical regimen of tizanidine plus diclofenac and a clinical study using tizanidine plus diclofenac to treat patient with low-back pain.

According to Wikipedia encyclopedia, "tizanidine" is the generic name of the compound of Formula  , also called "Zanaflex" or " Sirdalud". "Diclofenac" is the generic name of the compound of Formula  , a COX-2 inhibitor. See Wikipedia encyclopedia on-line version.

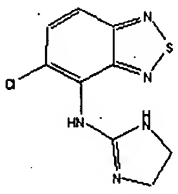
Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the *Sirdalud Study* and the instantly claimed inventions, is that the prior art reference teaches a COX-2 inhibitor "Diclofenac" compound with **R** as -H, but does not teach a compound wherein **R** as methyl or ethyl as claimed in the instant application.

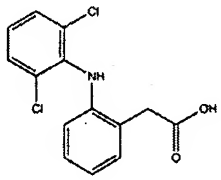
Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The instantly claimed pharmaceutical composition and methods of using the

Pharmaceutical composition for treating pain would have been obvious over the teaching disclosed in the *Sirdalud Study*. It is because that the pharmaceutical composition used in the *Sirdalud Study* comprises to active ingredients, i.e



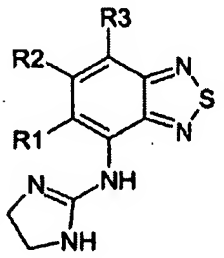
, and a COX-2 inhibitor



for treatment of pain. The difference between the prior art reference and the instantly claimed invention is the COX-2 inhibitor of formula V according to claim 7 of the instant application, wherein **R** is –H suggested by the prior art, and **R** is $-CH_3$, claimed according to claim 7. **R** is a phenyl substituent. The instantly claimed inventions and the prior art teaching are all related to the same utility for treating pain. One skilled in the art would have found the claimed compound prima facie obvious because it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lahr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e pharmacological use).

Claims 1, and 4-9 are rejected under 35 U.S.C. 103 (a) as unpatentable over a publication by Sirdalud Ternelin Asia-Pacific Study Group, *Current Therapeutic Research*, **1998**, Vol. 59, 1, pp. 13-22, ("the *Sirdalud Study*") in view of the teaching of COX-2 inhibitor of by Wikipedia encyclopedia, on-line edition.

Applicants' claims relate to a pharmaceutical composition for treatment of pain, which comprises in combination a benzothiadiazole derivative of formula (I)

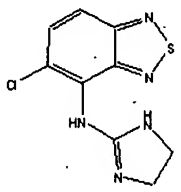


wherein each R1, R2 and R3 independently, is hydrogen, halogen, C_1-C_7 alkyl, C_1-C_7 alkoxy, nitro, cyano, hydroxy or C_1-C_7 alkylthio;
and a COX-2 inhibitor for simultaneous, sequential or separate use

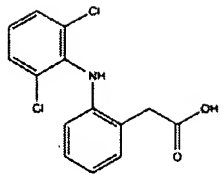
and a method of treating a patient suffering from pain comprising administering to the patient an effective amount of the pharmaceutical composition thereof according to claim 1.

Determination of the scope and content of the prior art (MPEP §2141.01)

The *Sirdalud Study* discloses a pharmaceutical regimen of tizanidine plus diclofenac and a clinical study using tizanidine plus diclofenac to treat patient with low-back pain.

According to Wikipedia encyclopedia, "tizanidine" is the generic name of the compound of Formula 

, also called "Zanaflex" or " Sirdalud". "Diclofenac"

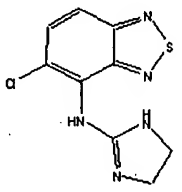
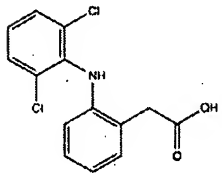


is the generic name of the compound of Formula , a COX-2 inhibitor. See Wikipedia encyclopedia on-line version.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the *Sirdalud Study* and the instantly claimed inventions, is that the prior art reference teaches a COX-2 inhibitor of "Diclofenac", but not teaching the other COX-2 inhibitors, such as Lumiracoxib, rofecoxib, etoricoxib, etc. according to claims 6 or 8.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The instantly claimed pharmaceutical composition and methods of using the Pharmaceutical composition for treating pain would have been obvious over the teaching disclosed in the *Sirdalud Study in view of the common skill in the related art of COX-2 inhibitor.* It is because that the pharmaceutical composition used in the *Sirdalud Study* comprises to active ingredients, i.e  , and a COX-2 inhibitor  for treatment of pain. Even though the prior art does not specifically teaches all the combination with COX-2 inhibitors, the difference however is obvious to one skilled in the art, since using COX-2 inhibitor to treat pain is suggested by the

Sirdalud Study reference and in view that the compound of claim 8 is Lumiracoxib as COX-2 inhibitor. See Lumiracoxib, Wikipedia, Encyclopedia on-line version. It has been obvious to combine two compositions taught by the prior art to be useful for the same purpose to form a third composition that is to be used for the very same purpose. *In re Kerkoyen*, 205 U.S.P.Q. 1069 (C.C.P.A. 1980).

Conclusion

- Claims 1; and 4-9 are rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached between 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER

Joseph K. McKane
Supervisory Patent Examiner
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